## EXAMINER'S AMENDMENT

1. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization of this Examiner's amendment was given in a telephone interview with Mr. John Isacson on September 17, 2010.

3. The Claims have been amended as follows:

9. (Currently Amended) A method for preparing an organ by perfusion prior to transplantation or storage of the organ comprising:

**[[**(I)**]]** providing a **[[**n**]]** preparation to ameliorate ischemic reperfusion injury;

**[[**prevention preparation for**]]** and

**[[**perfusion of**]]** perfusing an organ prior to transplantation or storage of the organ, wherein the **[[**ischemic reperfusion injury prevention**]]** preparation comprises:

**[[**(A)**]]** i) a soluble polypeptide **[[**,**]]** that has the amino acid sequence of SEQ ID NO:1 or

ii) a soluble polypeptide consisting of the amino acid sequence of amino acids 2-197 and 199-215 of SEQ ID NO:1, wherein the soluble polypeptide is conjugated to

myristoyl; and wherein perfusion comprises a non-reducing flush storage solution, wherein the flush storage solution is a perfusion solution; that comprises potassium citrate, sodium citrate, mannitol, and magnesium sulphate; and wherein the preparation maintains the complement inhibitor activity of the soluble polypeptide.

**[[**consists of: a fragment of complement receptor 1 (CR1) conjugated to myristoyl and a basic amino acid sequence, wherein said fragment has complement inhibitory activity, wherein the soluble polypeptide is SEQ ID NO:1, and wherein the CR1 fragment is amino acid residues 2-197 of SEQ ID NO:1 and the basic amino acid sequence is amino acid residues 199-215 of SEQ ID NO:1; and

(B) a physiologically acceptable and non-reducing flush storage

solution, wherein the flush storage solution is a kidney perfusion solution, that comprises potassium citrate, sodium citrate, mannitol, and magnesium sulphate; and

(11) perfusing the organ with the ischemic reperfusion injury prevention preparation, wherein the organ contains the ischemic reperfusion injury prevention preparation while isolated and prior to implantation, and the ischemic reperfusion injury prevention preparation retains the complement inhibitory activity of the soluble polypeptide. ]]

4. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

## *Conclusion*

5. Claims 9 and 19-21 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached at (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652

## DETAILED ACTION

### *Application Status*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 9, 2009 has been entered.

### *Claim Disposition*

2. Claims 9 and 19-21 are pending and under examination.

### *Specification*

3. The specification is objected to because of the following informalities:

The specification is objected to because the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the

claims are directed. The following is suggested: "A Method of Preparing an Organ by Perfusion".

***Information Disclosure Statement***

4. The Information Disclosure Statement filed on November 9, 2009 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

***Claim Objection***

5. Claim 9 is objected to because of the following informalities:

Claim 9 is objected to because item II has an extraneous period.

Claim 9 is objected to because the word 'complement' is misspelled as "compliment".

For clarity and precision of claim language it is suggested that the claim is amended to read,

"(Currently Amended) A method for preparing an organ by perfusion prior to transplantation or storage of the organ comprising:

(I) providing an ischemic reperfusion injury prevention preparation for perfusion of an organ prior to transplantation or storage of the organ, wherein the ischemic reperfusion injury prevention preparation comprises:

(A) a soluble [[derivative of a soluble]] polypeptide, that [[wherein the soluble derivative]] consists of:

a fragment of complement receptor 1 (CR1) conjugated to myristoyl and a basic amino acid sequence, wherein said fragment has [[having compliment]] complement inhibitory activity, [[and is]] wherein the soluble [[derivative]] polypeptide is [[set forth in]] SEQ ID NO: 1, and wherein the CR1 fragment is [[set forth at positions]] amino acid residues 2-197 of SEQ ID NO:1 and the basic amino acid sequence is [[set forth at positions]] amino acid residues 199-215 of SEQ ID NO:1; and

(B) a physiologically acceptable and non-reducing flush storage solution, wherein the [[physiologically acceptable]] flush storage solution is a kidney perfusion solution, that comprises potassium citrate, sodium citrate, mannitol, and magnesium sulphate; and

(II) perfusing the organ with the ischemic reperfusion injury prevention preparation, wherein the organ contains the ischemic reperfusion injury prevention preparation while isolated and prior to implantation, and the ischemic reperfusion injury prevention preparation retains the complement inhibitory activity of the soluble [[derivative.]] polypeptide.

Correction is required.

***Maintained-Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 9 and 19-21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (U.S. 6,713,606 B1) in view of the Baxter SOLTRAN solution product #FKB4708G and Varty et al.,(BMJ 1994, volume 308, page 575).

Smith et al. teach CR1 fragments that would inherently include a fragment of CR1-3. Further, Smith et al. teach soluble CR1 polypeptide that is derivatized with a myristoyl group (See column 17, line 55). At column 18, Smith et al. teach the use of peptides for Post-Ischemic Reperfusion Conditions. Smith et al. does not specifically teach SOLTRAN solution.

As supporting evidence to the fact that SOLTRAN is a popular and widely used solution that is used as physiologically acceptable flush solution, examiner included in the instant office action a copy of the Baxter's product that is sold as SOLTRAN solution and is commonly used in perfusion procedures.

Varty et al. teach that SOLTRAN produced by Baxter company was used in perfusion for organ donation purposes. (See third paragraph of the Abstract, on page 575 as included).

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to design a method for preparing an organ by perfusion prior to transplantation or storage of the organ that uses soluble CR1 polypeptide which includes a CR1-3 fragment that is derivatized with a myristoyl group and to administer such peptides to a patient or a transplant prior to implantation as taught by Smith et al. and to use in such a method the SOLTRAN product that is commonly used as a physiologically acceptable flush solution used in perfusion procedures as taught by Varty et al. One skilled in the art would be motivated to design such a method when SOLTRAN is utilized because such physiological solutions are commonly used in transplanting of different organs and preventing rejection of such organs. Therefore, the invention is *prima facie* obvious.

## ***Response to Arguments***

7. Applicant's arguments have been considered in full, however, are not persuasive. Applicants cites *KSR* and *Eisai Co*.; and argue that "when claims are directed to chemical entities, the inquiry turns to similarities and differences between the claimed subject matter and those of the prior art'. It is further stated that the "examiner has

focused on previous uses of SOLTRAN…The claimed invention is very different in that flush storage solution (i.e. SOLTRAN) is being used in an entirely different and non-obvious context, namely as a delivery vehicle for the soluble derivative to be carried to where it is needed in the organ".

Firstly, applicant is arguing a limitation not present in the claims as the instant method is directed to preparing an organ by perfusion not a delivery vehicle as stated by applicants. Secondly, applicant's admit that SOLTRAN is an example of the claimed 'flush storage solution' which is in the art. SOLTRAN, is a physiologically acceptable flush solution that is routinely used during perfusion procedures and the name itself is trademarked. The art also discloses the claimed CR1. Thirdly, the Smith reference remains relevant because in column 19, lines 60-67, Smith et al. teach a method of delaying hyperacute allograft or hyperacute xenograft rejection in a human or non-human, which receives a transplant by administering an effective amount of a soluble complement inhibitor, such as soluble CR1 polypeptide and derivative, where such administration maybe to the patient or by application to the transplant prior to implantation. Therefore, Smith et al. teach administration of CR1 fragments or derivatives to patients before surgery or to the organs to be transplanted themselves (instant claims 19-21).

Moreover, the peptides or derivatives of Smith et al. are conjugated to myristoyl, as claimed in amended claim 9. In addition, the Supreme Court pointed out in *KSR*, "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR, 127 S. Ct. at*

*1741*. The Court thus reasoned that the analysis under 35 U.S.C. 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the "inferences and creative steps that a person of ordinary skill in the art would employ." *Id. at 1741*. The Court further advised that "[a] person of ordinary skill is…a person of ordinary creativity, not automation." *Id. at 1742*. Therefore, the claimed invention was obvious to make and use at the time the invention was made and was *prima facie* obvious.

## ***Conclusion***

8. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to HOPE A. ROBINSON whose telephone number is (571)272-0957. The examiner can normally be reached on Monday-Friday 9:00-6:30 from 10:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Hope A. Robinson/

Primary Examiner, Art Unit 1652